Factors that Influence the Relative Potency of Diesel Exhaust Particles as Adjuvants in Allergic Airway Disease

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Studies have shown that diesel exhaust particles (DEP) worsen respiratory diseases, including allergic asthma. The adjuvant effects of DEP in the airways have been widely reported; however, the precise determinants and mechanisms of these effects are ill defined. Several factors may influence the ability of DEP to enhance allergic responses to respiratory allergens including physicochemical composition, size fraction, and genetic predisposition to the development of allergic asthma. Experimental data are presented here that demonstrate the influence of physical and chemical features on the relative toxicity of DEP. It is known that the composition of DEP may change with variations in conditions under which they are generated or collected. Two common DEP samples were compared to determine the differences in their chemical compositions and whether they would produce different levels of acute pulmonary toxicity and inflammation. Biomarkers of inflammation and acute lung injury were evaluated in CD-1 mice exposed to automobile-generated DEP (A-DEP; 4-cylinder Isuzu engine), National Institute of Standards Technology, standard reference material 2975 DEP (SRM-DEP; forklift), or saline (control). Scanning electron microscopy demonstrated that SRM-DEP had a greater range of particle sizes (<10 to >50μm) than A-DEP (>50μm). The A-DEP sample had approximately 1/6 the elemental carbon, yet 10 times more organic carbon and >10 times the percentage of extractable organic material compared to SRM-DEP. SRM-DEP stimulated a dose-dependent neutrophilic response, whereas A-DEP dose dependently activated macrophages and induced more than 2 times the amount of MIP-2 and TNFα compared with SRM-DEP. Both samples caused leakage of microalbumin into the lung lumen. This work was completed through partnerships among NHEERL, NRMRL (RTP, NC), and NIES (Tskuba, Japan). From these studies, we concluded that differences in proinflammatory responses induced by the two DEP samples were associated with differences in physicochemical features of each sample. These studies have allowed us to identify the physical and chemical properties of DEP that convey the potential to enhance the risk of developing asthma or to exacerbate pre-existing disease. By understanding the influence of a variety of factors on the potency of DEP as an allergic adjuvant, it will be possible to make recommendations on how to minimize health effects due to exposures to DEP. The information gained from these studies has provided a rationale for further investigation into the underlying cellular and molecular mechanisms of diesel-enhanced allergic airways disease.